

B1
Current

wherein the antibody comprises an amino acid sequence shown in SEQ ID NO: 8.

Please replace the paragraph beginning on page 4, line 14 with the following paragraph:

B2

In yet another aspect, the invention pertains to a humanized antibody that is specifically reactive with human CTLA4, wherein the antibody comprises an amino acid sequence shown in SEQ ID NO: 10.

Please replace the paragraph beginning on page 7, line 23 with the following paragraph:

B3

As used herein, the term "costimulatory receptor" includes receptors which transmit a costimulatory signal to a immune cell, e.g., CD28. As used herein, the term "inhibitory receptors" includes receptors which transmit a negative signal to an immune cell (e.g., CTLA4). An inhibitory signal as transduced by an inhibitory receptor can occur even if a costimulatory receptor (such as CD28) is not present on the immune cell and, thus, is not simply a function of competition between inhibitory receptors and costimulatory receptors for binding of costimulatory molecules (Fallarino *et al.* (1998) *J. Exp. Med.* 188:205). Transmission of an inhibitory signal to an immune cell can result in unresponsiveness or anergy or programmed cell death in the immune cell.

Please replace the paragraph beginning on page 68, line 3 with the following paragraph:

Antibodies that mimic interaction of CTLA4 with a costimulatory molecule (e.g., CTLA4 activating antibodies or multivalently presented antibodies) can be identified by their ability to inhibit immune cell proliferation and/or effector

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function or to induce anergy when needed to an *in vitro* assay. For example, cells can be cultured in the presence of an agent that stimulates signal transduction via an activating receptor. A number of art recognized readouts of cell activation can be employed to measure the ability of an antibody to transmit a negative signal, e.g., by measuring its effect on cell proliferation or T cell effector function (e.g., cytokine production) in the presence of the activating agent. The ability of a test agent to block this activation can be readily determined by measuring the ability of the agent to effect a decrease in proliferation or effector function being measured.

IN THE CLAIMS:

Please cancel claim 12 without prejudice.

Please amend claims 1, 7, 14, and 15 as follows:

B5
1. (Amended) An antibody-toxic moiety conjugate comprising an antibody that specifically recognizes (a) at least one of a B7 costimulatory molecule and a costimulatory receptor expressed on an activated T cell and (b) a toxic moiety.

B6
7. (Amended) The antibody-toxic moiety conjugate of claim 2, wherein the substitution of amino acid 83 in the amino acid sequence of human CTLA4 shown in SEQ ID NO: 2 results in reduced binding of the antibody by at least about 80% compared to an antibody without the substitution of amino acid 83.

B7
14. (Amended) A humanized antibody that is specifically reactive with human CTLA4, wherein the antibody comprises the amino acid sequence shown in SEQ ID NO: 8.

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